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The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte STEFANO CARLINO

Appeal 2010-008871
Application 10/523,657
Technology Center 1600

Before LORA M. GREEN, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's rejection of claims 1 and 4-9. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF THE CASE

Claim 1 is the only independent claim on appeal, and reads as follows:

1. A process for preparing a sterile ready-to-use aqueous pharmaceutical formulation comprising a high molecular weight hyaluronic acid salt (HA) at a specified concentration, comprising the steps of:

- providing an aqueous formulation comprising high molecular weight HA at a concentration of less than the specified concentration;
- passing said aqueous formulation through a filter having a pore size less than 0.45 μm; and greater than 0.1 μm;
- concentrating said aqueous formulation by applying a vacuum and boiling off water until said specified concentration is reached; and
- after the concentration step, filling the pharmaceutical formulation directly into sterile recipients ready for pharmaceutical use, or into sterile tanks and subsequently directly into sterile recipients ready for pharmaceutical use.

The following grounds of rejection are before us for review:

I. Claims 1 and 4-9 stand rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,489,467 B1 to Carlino (issued December 3, 2002) as combined with Perbellini (U.S. Patent No. 5,503,848, issued April 2, 1996).

II. Claims 1 and 4-9 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Carlino (U.S. Patent No. 6,489,467) or Carlino (WO 00/44925, published August 3, 2000) and Perbellini.

We reverse.

ISSUE

Has the Examiner established by a preponderance of the evidence that the combination of claims 1-23 of U.S. Patent No. 6,489,467, Carlino (U.S. Patent No. 6,489,467) or Carlino (WO 00/44925) with Perbellini renders the method of independent claim 1 obvious?

FINDINGS OF FACT

FF1 The Specification teaches that the "invention relates to a process for preparing a sterile high molecular weight hyaluronic acid salt as a final formulation for pharmaceutical use." (Spec. 1.)

FF2 The Specification notes:

> Industrial extraction and purification processes of hyaluronic acid typically produce hyaluronic acid salts, such as sodium hyaluronate, in the form of a dried powder. The purified pharmaceutical grade dried power may be used for preparing, for example, aqueous pharmaceutical formulations for the various pharmaceutical uses such as interarticular injection, eye drops or vitreous humor replacement.
>
> A common industrial process for preparing ready-to-use pharmaceutical formulations comprises the mixing of a defined quantity in weight of sodium hyaluronate with a precise volume of water and, as the case may be, salt such as sodium chloride and buffers such as phosphates and other excipients. As the concentration and composition of the formulation for pharmaceutical use should remain within a narrowly defined range, the various components of the formulation are carefully measured. The formulation is then filled into recipients such as syringes and vials of defined dosages ready for use. Subsequent to filling of the recipients, the formulation is sterilized by autoclave typically at around 121° C for fifteen minutes or more.

(Spec. 2-3.)

FF3 According to the Specification:

> During the concentrating step after filtration, the concentration of HA may be monitored in real time in order to stop the vacuum boiling when the specified concentration for the ready-to-use pharmaceutical formulation is reached. The monitoring or measuring process may advantageously be carried out with a spectrophotometer with the sensing beam placed in the formulation, the absorption of radiation in the ultraviolet range (UV) being proportional to the HA concentration. *A particularly advantageous feature of this invention is that it obviates the need to mix exact quantities of water and hyaluronic acid to obtain the specified concentration and ensure that such concentration is maintained through the process.* Instead, the initial HA and water mix has an approximate concentration lower than the final formulation, thus simplifying the process.

(*Id.* at 6-7 (emphasis added).)

FF4 The Examiner's statement of the rejections may be found at pages 3-5 of the Answer.

FF5 The teaching and claims of U.S. Patent No. 6,489,467 are essentially the same as the teachings of Carlino (WO 00/44925). We thus focus our analysis on Carlino (WO 00/44925).

FF6 The Examiner finds that Carlino discloses "a process for preparing a purified hyaluronic acid formulation comprising sterilizing hyaluronic acid by passing an aqueous formulation through a filter having a pore size of 0.2 um." (Ans. 5 (citing Carlino, p. 10).)

FF7 Carlino teaches a process of preparing a dry powder of hyaluronic acid, wherein the an aqueous solution is filter sterilized, and concentrated

using a filter having a 5,000-10,000 Daltons molecular weight cutoff. (Carlino, p.10.)

FF8 The Examiner notes that Carlino does not disclose "the step of concentrating said formulation under vacuum until a desired concentration is achieved." (Ans. 5.)

FF9 The Examiner finds that Perbellini discloses "preparation of a hyaluronic acid formulation wherein said formulation is subjected to a vacuum until a desired concentration is achieved and parceling said formulation into a sterile containers." (*Id.*)

FF10 Specifically, Perbellini teaches the following preparation process for preparing a spongy material that consists of hyaluronic acid or its derivatives and appears from a macroscopic point of view as a highly microporous spongy little disk:

> 1. Dissolution of the active principle
>
> In a suitable apparatus, equipped with a heating system, suitable stirring and vacuum/nitrogen pressure/sterile filtrate system, hyaluronic acid, or one of its estereal derivatives, is dissolved in water for injectable preparations, so as to reach a concentration ranging between 1 mg/ml and 40 mg/ml.
>
> 2. Solution filtration
>
> The solution containing hyaluronic sodium salt is filtered suitably through a sterilizing membrane, having a porosity of 0.2 micrometers, afterwards it is collected in a sterile environment.
>
> 3. Solution distribution
>
> The filtered solution is parcelled out in a sterile environment, into suitable sterile containers, such as tiny bottles, blisters and the like, by dosing the solution so as to achieve 10 mg of active principle in each container.
>
> 4. Lyophilization

> The containers, after having been filled up, are put into a lyophilization apparatus and the product is frozen to a temperature ranging between 0° C. and -90° C.; the temperature decrease for achieving the freezing is captied [sic] out at rates ranging between 1° C. every 20 seconds and 1° C. every 3 hours.
>
> Drying step by high vacuum (residual vacuum in the chamber ranging between 1000 and 1Hg mm) and heating step with plate temperature ranging between -90° C. and +60° C., follow.
>
> * * * *
>
> At the end of the lyophilization the tiny bottles are stoppered in a sterile way.

(Perbellini, col. 10, ll. 21-57.)

FF11 Thus, Perbellini, while teaching a step of vacuum filtration, as well as a step of lyophilization, does not teach a step of concentrating an aqueous solution of HA by applying a vacuum and boiling off water until a more concentrated aqueous solution of HA is obtained.

FF12 The Examiner concludes it would gave been obvious to use the process of Perbellini in the process of Carlino "in order to achieve a formulation which is suitable to the [sic, be] parceled out into sterile containers." (Ans. 5.)

PRINCIPLES OF LAW

> If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the preamble is "necessary to give life, meaning, and vitality" to the claim, then the claim preamble should be construed as if in the balance of the claim. . . . If, however, the body of the claim fully and intrinsically sets forth the complete invention, including all of its limitations, and the preamble offers no distinct definition of

> any of the the claimed invention's limitations, but rather merely states, for example, the purpose of intended use of the invention, then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation.

Pitney Bowes, Inc. v. Hewlett Packard Co., 182 F.3d 1298, 1305 (Fed. Cir. 1999). Moreover, while limitations from the Specification are not to be read into the claim, "[i]t is entirely proper to use the specification to interpret what . . . [is] meant by a word or a phrase in the claim." *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1433 (Fed. Cir. 1988). *See also In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

In addition, the Examiner must consider all of the claim limitations in setting forth a rejection over the prior art. *See, e.g., In re Geerdes*, 491 F.2d 1260, 1262-63 (CCPA 1974) (in considering grounds of rejection, "every limitation in the claim must be given effect rather than considering one in isolation from the others.").

ANALYSIS

We start with claim interpretation. Claim 1 is drawn to a "process for preparing a sterile ready-to-use aqueous pharmaceutical formulation comprising a high molecular weight hyaluronic acid salt (HA) at a specified concentration," wherein an aqueous formulation of HA is concentrated under vacuum by boiling off water, and then after the concentration step, "filling the pharmaceutical formulation directly into sterile recipients ready for pharmaceutical use, or into sterile tanks and subsequently directly into sterile recipients ready for pharmaceutical use." In light of the teachings of

the Specification, we interpret the process of claim 1 as requiring the HA to be always in an aqueous solution. Stated in other terms, we interpret the claim as excluding a step of concentrating the HA by drying the HA to a powder and adding back water.

Appellant argues that Perbellini "does not disclose any step for concentration of a filter-sterilized solution of HA, by applying a vacuum and boiling off water until a specified concentration is reached, as required by the claims of the present invention." (App. Br. 15.) We agree. As noted above, Perbellini's process involves preparing an HA solution from a dried product, which the claims exclude (*See* FF10 and 11.) As the Examiner's fact-finding is incorrect, and in view of the claim interpretation set forth above, we are compelled to reverse the rejections on appeal.

CONCLUSION OF LAW

We conclude that the Examiner has not established by a preponderance of the evidence that the combination of claims 1-23 of U.S. Patent No. 6,489,467, Carlino (U.S. Patent No. 6,489,467) or Carlino (WO 00/44925) with Perbellini renders the method of independent claim 1 obvious. We are thus compelled to reverse both rejections on appeal.

REVERSED

cdc

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